REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following commentary.

I. Status of the Claims

Claims 3, 5, 7-19 were cancelled previously. Claims 1, 2, 4, and 6 are withdrawn by the Examiner for directing to non-elected species. Applicants respectfully submit that upon allowance of a generic claim, additional species should be rejoined for examination in this application. Claims 22 and 23 have been amended to delete the recitation of hybridoma FERM BP-7840.

Applicants acknowledge the finality of this office action. Nevertheless, because the amendments are made to delete subject matter, and because the amendments place the application either in condition for allowance or at least in better condition for appeal, Applicants respectfully request entry of this amendment. Upon entry, claims 1, 2, 4, 6, and 20-25 will be pending, with claims 1, 2, 4, and 6 withdrawn.

II. Rejection of Claims under 35 U.S.C. § 102(b)

The Examiner rejected claims 23-25 for alleged anticipation by PCT publication WO 01/66596 by Itoh et al. ("Itoh"), as evidenced by Yu *et al., Endocrinology* 146: 4647-56, 2005, Mohammadi *et al., Cytokin Growth Factor Rev.* 16: 107-37, 2005. Applicants respectfully traverse the rejection.

In particular, the Examiner contends that the claim limitation of "which can neutralize FGF-23 activity" fails to distinguish the claimed antibodies from the antibodies of the Itoh publication. To this end, the rationale advanced by the Examiner rests on an assumption that Itoh's antibodies "would inherently possess the property" of the claimed antibody because (i) Itoh's antibodies bind the same sequence of amino acid 1 to around 179 of FGF-23, (ii) Itoh's

antibodies can be used to treat hypophosphatemic diseases, and (iii) additional scientific literature shows the highly conserved receptor binding surface of the FGF molecule (final office action, 4th and 6th paragraphs).

Contrary to the Examiner's assertion, however, antibodies that can bind to the sequence of amino acid residues 1-179 of FGF-23 do not necessarily (or "inherently") have the property of neutralizing the FGF-23 activity.

In substantiation of this point, Applicants submit accompanying Exhibit A, which presents the results of studies performed by the inventors into different antibodies, such as 2A2B antibody and 2C3B antibody, that neutralize FGF-23 activity.

The binding sequences of both 2A2B antibody and 2C3B antibody are disclosed in the specification. For example, the specification teaches that 2A2B antibody recognizes a site corresponding to amino acid residues 148-163 of SEQ ID NO: 1 (FGF-23) (*see* page 68, lines 7-9) and that 2C3B antibody has a recognition sequence within the N-terminal of the protein, corresponding to amino acid residues 25-179 of SEQ ID NO: 1 (*see* page 68, lines 14-17). Accordingly, both antibodies bind to the same sequence of amino acid residues 1-179 of FGF-23.

Exhibit A demonstrates that 2A2B antibody and 2C3B antibody display quite different FGF-23 neutralizing activities. As shown in figures 1 and 2, 2C3B antibody exhibits significant neutralizing activity at a low concentration of 1 μg/ml to both a native FGF-23 protein and a mutant FGF-23 protein having glutamine substitutions for 176th and 179th arginines. In contrast, 2A2B antibody does not show much neutralizing activity to either the native or the mutant protein even at a concentration as high as 10 μg/ml.

Thus, antibodies binding to the sequence of amino acid residues 1-179 of FGF-23 do not "inherently" possess the property of neutralizing FGF-23 activity. Because the Examiner's rejection is based on a faulty rationale, withdrawal of the anticipation rejection is warranted.

III. Rejection of Claims under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 22, 23 and 25 for alleged lack of enablement. Applicants respectfully traverse the rejection.

Specifically, the Examiner contends that the specification "does not reasonably provide enablement for a pharmaceutical composition of an antibody produced by FERM BP-7840" (final office action, page 6, second paragraph). Without acquiescing to the stated rationale for the rejection, Applicants choose to advance the prosecution by amending claims 22 and 23 to delete the recitation of FERM BP-7840. Accordingly, the basis for the rejection is obviated.

IV. Provisional Double Patenting Rejection

The Examiner provisionally rejected claims 23-25 on the ground of nonstatutory obviousness-type double patenting over claims 10 and 12-15 of copending U.S. Patent Application No. 10/344,339, in view of Yu *et al., Endocrinology* 146:4647-4656, 2005, Mohammadi *et al., Cytokin Growth Factor Rev.* 16:107-137, 2005, and Bost *et al., Immunol. Invest.* 17:577-586, 1988.

Applicants choose to defer any action until the Examiner indicates that the claims are otherwise allowable.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-

0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, Applicants hereby petition for such extension under 37 CFR §1.136 and authorize payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

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